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<input type="checkbox"/>	L2	L1 same wollinella	0
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<input type="checkbox"/>	L6	L1 same pasteurella	0
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<input type="checkbox"/>	L9	L1 same salmonell\$	0
<input type="checkbox"/>	L10	phsa or phsb or phsc or phsd or phsabcd	93
<input type="checkbox"/>	L11	phsa or phsb or phsc or phsd or phsabcd	93
<input type="checkbox"/>	L12	L11 and salmonell\$	5

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- ☐ 1. [6780405](#). 28 Apr 00; 24 Aug 04. Regulated antigen delivery system (RADS). [Curtiss, III](#); Roy, et al. 424/93.1; 424/200.1 424/93.2 424/93.4 435/252.3 435/320.1. A01N063/00 A01N065/00 A61K039/02 C12N001/20 C12N015/00.
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- ☐ 2. [6610529](#). 06 Dec 96; 26 Aug 03. Recombinant bacterial system with environmentally limited viability. [Curtiss, III](#); Roy, et al. 435/252.3; 424/257.1 424/258.1 424/93.1 424/93.2 424/93.48 435/442 435/471 435/481 435/69.1. C12N001/21 A01N063/00 A61K039/108 C12P012/06.
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- ☐ 3. [6383496](#). 18 May 99; 07 May 02. Recombinant vaccines comprising immunogenic attenuated bacteria having RPOS positive phenotype. [Curtiss, III](#); Roy, et al. 424/200.1; 424/258.1 424/93.2 435/252.3 435/252.8 435/471 435/897. A61K039/02 A61K048/00 C12N015/74 C12N001/21.
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- ☐ 4. [6024961](#). 14 Nov 97; 15 Feb 00. Recombinant avirulent immunogenic *S typhi* having rpos positive phenotype. [Curtiss, III](#); Roy, et al. 424/200.1; 424/93.2 435/252.3 435/252.8 435/27 435/29 435/4 435/471. A61K039/02 A61K039/112 A61K039/116 A61K039/295 C12N001/21.
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- ☐ 5. [5888799](#). 02 May 94; 30 Mar 99. Recombinant avirulent bacterial antigen delivery system. [Curtiss, III](#); Roy. 435/252.3; 424/184.1 424/257.1 424/258.1 435/243 435/252.8. C12N001/20 C12N001/00 A61K039/108 A61K039/112.
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- ☐ 6. [5855880](#). 05 Feb 96; 05 Jan 99. Avirulent microbes and uses therefor. [Curtiss, III](#); Roy, et al. 424/93.2; 424/184.1 424/200.1 424/235.1 424/257.1 424/258.1 424/93.48 435/252.3 435/252.33 435/320.1 435/879. A61K039/02 A61K039/112 C12N001/21.
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- ☐ 7. [5855879](#). 10 Mar 94; 05 Jan 99. Avirulent microbes and uses therefor. [Curtiss, III](#); Roy. 424/93.2; 424/184.1 424/200.1 424/235.1 424/257.1 424/258.1 424/93.48 435/252.3 435/252.33 435/320.1 435/879. A61K039/02 A61K039/112 C12N001/21.
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- ☐ 8. [5840483](#). 07 Jun 95; 24 Nov 98. Method of maintaining a desired recombinant gene in a genetic population of cells. [Curtiss, III](#); Roy. 435/6; 435/252.3 435/252.33 435/320.1. C12Q001/68.
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- ☐ 9. [5686079](#). 01 Jun 95; 11 Nov 97. Oral immunization by transgenic plants. [Curtiss, III](#); Roy, et al. 424/234.1; 424/184.1 435/69.1 435/69.3. A61K039/02 C12N015/31 C12N005/10 A01H005/00.
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- ☐ 10. [5679880](#). 01 Jun 95; 21 Oct 97. Oral immunization by transgenic plants. [Curtiss, III](#); Roy, et al. 800/298; 424/234.1 424/439 424/93.7 435/252.3 435/320.1 435/419 435/69.3 536/23.7. C12N015/31 C12N005/10 A01H005/00 A61K039/02.
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- ☐ 11. [5672345](#). 10 Mar 95; 30 Sep 97. Selective maintenance of a recombinant gene in a population of vaccine cells. [Curtiss, III](#); Roy. 424/93.2; 435/252.3 435/69.1 435/71.2. A61K039/02 C12P021/00 C12N015/00 C12N001/21.
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- ☐ 12. [5656488](#). 01 Apr 94; 12 Aug 97. Recombinant avirulent *salmonella* antifertility vaccines. [Curtiss, III](#); Roy, et al. 435/252.33; 424/184.1 424/200.1 435/252.3 435/252.8 435/69.3 530/395. C12N001/21 A61K045/00.
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☐ 13. 5654184. 01 Jun 95; 05 Aug 97. Oral immunization by transgenic plants. Curtiss, III; Roy, et al. 424/234.1; 424/439 424/93.7 435/252.3 435/320.1 435/69.3 536/23.7. C12N015/31 C12N005/10 A01H005/00 A61K039/02.

☐ 14. 5468485. 18 Feb 93; 21 Nov 95. Avirulent microbes and uses therefor. Curtiss, III; Roy. 424/184.1; 424/200.1 424/93.1 424/93.2 435/252.3 435/252.33 435/252.8 435/69.1 435/71.1. A61K039/00 A61K039/02 C12N001/21 C12N015/00.

☐ 15. 5424065. 19 Nov 92; 13 Jun 95. Vaccines containing avirulent phop-type microorganisms. Curtiss, III; Roy, et al. 424/93.2; 424/184.1 424/93.48 435/252.3 435/252.8 435/69.1 435/71.1. A61K039/02 C12N001/21.

☐ 16. 5387744. 07 Jul 93; 07 Feb 95. Avirulent microbes and uses therefor: Salmonella typhi. Curtiss, III; Roy, et al. 424/258.1; 435/252.3 435/252.33 435/320.1 435/879. A61K039/112 C12N001/21.

☐ 17. 5294441. 07 Nov 91; 15 Mar 94. Avirulent microbes and uses therefor: salmonella typhi. Curtiss, III; Roy. 424/200.1; 424/235.1 424/258.1 435/252.3 435/252.33 435/320.1 435/879. A61K039/112 C12N001/21.

☐ 18. 4968619. 17 Oct 83; 06 Nov 90. Modified microorganisms and method of preparing and using same. Curtiss, III; Roy. 435/252.33; 435/252.8 435/849. C12R001/185 C12N015/00.

☐ 19. 4888170. 09 Sep 85; 19 Dec 89. Vaccines obtained from antigenic gene products of recombinant genes. Curtiss, III; Roy. 424/200.1; 424/244.1 424/258.1 435/252.3 435/252.8. C12N001/20 C12N001/42 A61K039/112 A61K039/09.

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L6: Entry 1 of 20

File: USPT

Aug 24, 2004

US-PAT-NO: 6780405

DOCUMENT-IDENTIFIER: US 6780405 B1

TITLE: Regulated antigen delivery system (RADS)

DATE-ISSUED: August 24, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Curtiss, III; Roy</u>	St. Louis	MO		
Tinge; Steven A.	Belleville	IL		

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Avant Immunotherapeutics, Inc.	Needham	MA			02

APPL-NO: 09/ 560539 [PALM]

DATE FILED: April 28, 2000

INT-CL: [07] A01 N 63/00, A01 N 65/00, A61 K 39/02, C12 N 1/20, C12 N 15/00

US-CL-ISSUED: 424/93.1; 424/93.2, 424/93.4, 424/200.1, 435/252.3, 435/320.1

US-CL-CURRENT: 424/93.1; 424/200.1, 424/93.2, 424/93.4, 435/252.3, 435/320.1

FIELD-OF-SEARCH: 424/93.1, 424/93.2, 424/93.4, 424/200.1, 435/252.3, 435/320.1

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

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<input type="checkbox"/>	<u>4424065</u>	January 1984	Langhoff et al.	
<input type="checkbox"/>	<u>4837151</u>	June 1989	Stocker	
<input type="checkbox"/>	<u>4888170</u>	December 1989	Curtiss, III	
<input type="checkbox"/>	<u>5015573</u>	May 1991	Yarranton et al.	
<input type="checkbox"/>	<u>5028530</u>	July 1991	Lai et al.	
<input type="checkbox"/>	<u>5278744</u>	January 1994	Geboers et al.	
<input type="checkbox"/>	<u>5294441</u>	March 1994	Curtiss, III	
	<u>5389368</u>	February 1995	Curtiss, III	

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<input type="checkbox"/>	<u>5424065</u>	June 1995	Curtiss, III
<input type="checkbox"/>	<u>5468485</u>	November 1995	Curtiss, III
<input type="checkbox"/>	<u>5656488</u>	August 1997	Curtiss, III
<input type="checkbox"/>	<u>5672345</u>	September 1997	Curtiss, III
<input type="checkbox"/>	<u>5674746</u>	October 1997	Morris
<input type="checkbox"/>	<u>5840483</u>	November 1998	Curtiss, III
<input type="checkbox"/>	<u>5855879</u>	January 1999	Curtiss III
<input type="checkbox"/>	<u>5855880</u>	January 1999	Curtiss, III
<input type="checkbox"/>	<u>5888790</u>	March 1999	Cahoon et al.
<input type="checkbox"/>	<u>6024961</u>	February 2000	Curtiss, III

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
9640947	June 1996	WO	

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ART-UNIT: 1645

PRIMARY-EXAMINER: Navarro; Mark

ATTY-AGENT-FIRM: Yankwich & Associates Yankwich; Leon R. Wesolowski; Michael R.

ABSTRACT:

We describe a regulated antigen delivery system (RADS) that has (a) a vector that includes (1) a gene encoding a desired gene product operably linked to a control sequence, (2) an origin of replication conferring vector replication using DNA polymerase III, and (3) an origin of replication conferring vector replication using DNA polymerase I, where the second origin of replication is operably linked to a control sequence that is repressible by a repressor. The RADS microorganism also has a gene encoding a repressor, operably linked to an activatable control sequence. The RADS described provide high levels of the desired gene product after repression of the high copy number origin of replication is lifted. The RADS are particularly useful as live bacterial vaccines. Also described is a delayed RADS system, in which there is a delay before the high copy number origin is expressed after the repression is lifted. The delayed RADS is also particularly useful for live bacterial vaccines. Also described are several control elements useful for these systems, as well as methods for providing immunity to a pathogen in a vertebrate immunized with the RADS microorganisms.

24 Claims, 23 Drawing figures